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Growth Hormone and Mecasermin Review

Growth Hormone

- **Multiple FDA approved GH products**
 - Are they identical, can one be used to treat all approved indications?



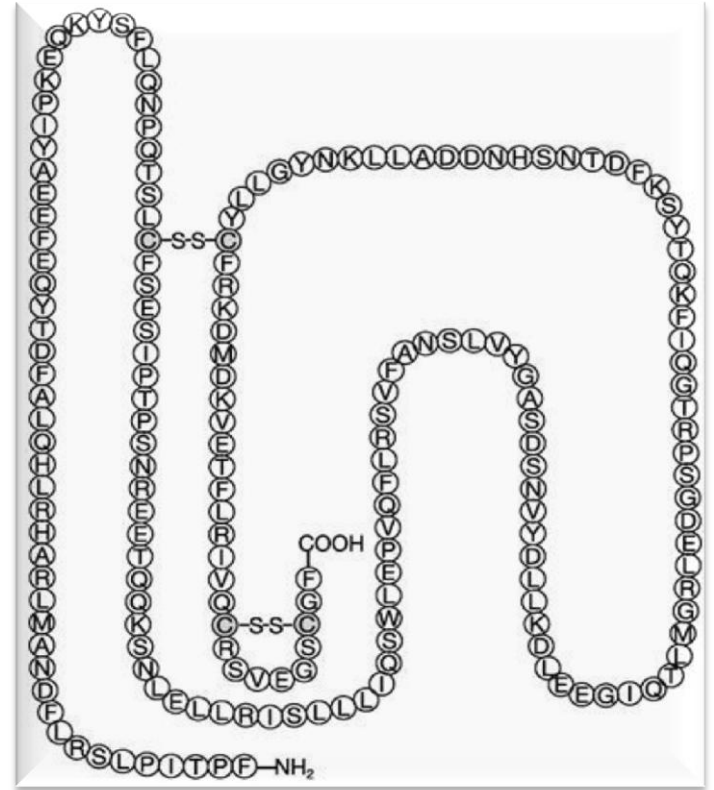
Background

■ GH therapy Prior to 1985

- Obtained from cadaver pituitaries
- Available in limited quantities

■ 1985

- Contaminates likely the cause of death in three young men
 - Prions → → → Creutzfeldt-Jakob
 - Likely the cause of Creutzfeldt-Jakob disease in more than 50 patients since 1985
- Availability of biosynthetic recombinant human GH
 - Somatropin
 - Amino acid sequence identical to GH of pituitary origin
 - Unlimited supply compared to cadaveric GH



Physiological Effects and Benefits of GH Therapy

■ Linear Growth

- Stimulates hepatic production of IGF1

■ Anabolic and lipolytic effects

- Lipolysis
- Protein synthesis
- Increased lean body mass
- loss of visceral adipose tissue

■ Cardiac function

- ↑LV mass, LVEDV, SV

■ Bone turnover

- Increasing bone density

■ Insulin antagonism

■ Improved mood/motivation and QOL

■ Enhanced exercise capacity



Growth Hormone - Indications

| BRAND | Growth Hormone Deficiency | Growth Hormone Deficiency (Adults) | Growth Failure-Renal Failure | HIV Wasting (Adults and Peds) | HIV Fat Mal-distribution (Adults) | Idiopathic Short Stature | Prader-Willi | Short Bowel (Adults) | Turner | Small for Gestational Age | Noonan | Short Stature - SHOX |
|-------------|---------------------------|------------------------------------|------------------------------|-------------------------------|-----------------------------------|--------------------------|--------------|----------------------|--------|---------------------------|--------|----------------------|
| GENOTROPIN | X | X | | | | X | X | | X | X | | |
| HUMATROPE | X | X | | | | X | | | X | X | | X |
| NORDITROPIN | X | X | | | | | | | X | X | X | |
| NUTROPIN | X | X | X | | | X | | | X | | | |
| OMNITROPE | X | X | | | | X | X | | X | X | | |
| SAIZEN | X | X | | | | | | | | | | |
| SEROSTIM | | | | X | | | | | | | | |
| TEV-TROPIN | X | | | | | | | | | | | |
| ZORBTIVE | | | | | | | | X | | | | |

X = FDA approved use

Clinical Guideline Review: Children

■ Diagnosis

- Height, height velocity
- Bone age
- GH levels/stimulation testing
- IGF-1/IGFBP3 levels
- Genetic testing
- Intracranial Lesion
- Multiple pituitary hormone deficiencies

■ FDA Approved Indications

■ Dosing

- 0.175-0.35 mg/kg/wk

■ Contraindications

- Active malignancy, or less than one year after treatment
- Diabetic retinopathy

■ Monitoring

- Height velocity, linear growth, HbA1c, IGF-1, T₄, TSH

■ Discontinuation

- Completion of growth
 - Final height or epiphyseal closure
- No growth increase x 1 year



GH Clinical Guideline Review: Adults

■ **Diagnosis**

- 2 GH stimulation tests, and IGF1 levels,
 - continuation therapy
- Hypothalamic-pituitary structural lesions
- Panhypopituitarism
- Traumatic brain injury and aneurysmal subarachnoid hemorrhage

■ **FDA approved indications only**

- **No Evidence to suggest treatment of aging or sports enhancement**

■ **Dosing**

- 0.1 – 0.5 mg/day

■ **Contraindications**

- Active Malignancy

■ **Monitoring**

- **IGF, HbA1c**, BMI, waist circumference, waist to hip ratio, fasting lipid panel, T4, cosyntropin stimulation test, estrogen, QOL assessment every 6 to 12 months.

■ **Discontinuations**

- No established length of therapy
 - Indefinitely
- Discontinue after 2 years if no benefits experienced

Safety Issues

■ **Contraindications**

- active malignancy
- active proliferative, preproliferative, or severe nonproliferative diabetic retinopathy

■ **Metabolic complications**

- Hyperglycemia, hypothyroidism
- Increase incidence of type 2 DM in GH-treated adults and children

- Body fluid retention, peripheral edema
- Intracranial hypertension
- Arthralgia, myalgia, headache
- Carpal tunnel syndrome, paresthesias, and hypoesthesia
- slipped capital femoral epiphysis in children
- Pancreatitis

Pipeline...

- **Long-Acting Growth Hormone**
 - Once weekly dosing
- **Novo Nordisk**
 - Pegylated
 - Currently in Phase I and II trials for both adults and children
- **LGLS and Biopartners**
 - Sustained release formulation
 - Positive Phase III data in both adults and children

Mecasermin (Increlex)

- Recombinant human insulin-like growth factor-1 (IGF1)
- Mediates anabolic and growth-promoting effects of GH
 - Stimulates the uptake of glucose, lipids and protein to support growing tissues.
- Indications
 - Severe primary insulin-like growth factor deficiency (Primary IGFD)
 - Patients with growth hormone gene deletion who develop neutralizing antibodies to growth hormone
- Dosing
 - ≥ 2 years: 0.12 mg/kg SC bid
- Side Effects
 - Hypoglycemia
 - Administer within 20 minutes before or after eating
- Contraindications
 - Suspected or active neoplastic Disease
- Has not been studied in adults over 22 years of age.
 - Average age of study subjects:
 - 6.7 ± 3.8 years

Questions?

